

# Polycystic Ovary Syndrome

Case Conference

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## Ms. G Presentation - HPI

- 27 y/o Russian woman, G2P0020 (tabs)
- Irregular menses and facial hair since menarche (age 10)
- Periods are q 35-90 days, occasional spotting
- Currently sexually active, monogamous, Uses IUD
- Facial hair bothers her most.

# Presentation - FHX

- Father and Grandfather with DM type II
- Mom with hirsutism

# Medications

- None

## Presentation - Physical Exam

- Vitals: BP 120/70, 5'1", 214 lbs
- Heent: Facial hair under chin and slightly on cheeks
- Skin: fair complexion, no chest or back hair, no striae
- GU: Normal female genitalia inside and out, slight abdominal escutcheon (es-kuch'en: the pattern pubic hair distribution), IUD in place

# Diagnosis

- Clinically seems likely to be polycystic ovarian syndrome
- How can I be sure???

# Polycystic Ovarian Syndrome a.k.a. Stein- Leventhal Syndrome

- Discussed in literature for centuries, characterized by S and L 1935
- Epidemiology:
  - 6% prevalence in women of reproductive age
  - some variation by ethnic group
    - higher in Spain and Greece
  - some small studies suggest increased prevalence in women with Diabetes and Epilepsy

# Definition

1990 National Institute of Health Conference  
on PCOS defines by two minimal criteria  
not explained by other causes

– Chronic oligo or anovulation

- cycle length  $>35$  days or  $<8$  cycles/year

– Hyperandrogenism

- clinically or lab tests
- clinical features include hirsutism, acne, alopecia, acanthosis nigricans

# Clinical Presentation

- Menstrual Irregularity
- Obesity: waist:hip ratio  $>.85$
- Hirsutism/acne
- Occasional Acanthosis Nigrans
- Less common: Clitoromegaly, deep voice, temporal balding



**Obesity and cushingoid appearance in PCOS** 32 year-old woman with exogenous obesity and polycystic ovarian syndrome. The patient has changes similar to those in Cushing's syndrome including "moon" face, facial plethora, mild acne, hirsutism, and increased supraclavicular fat pads. Her cortisol secretion was normal. Courtesy of David N Orth, MD.

# Differential Diagnosis

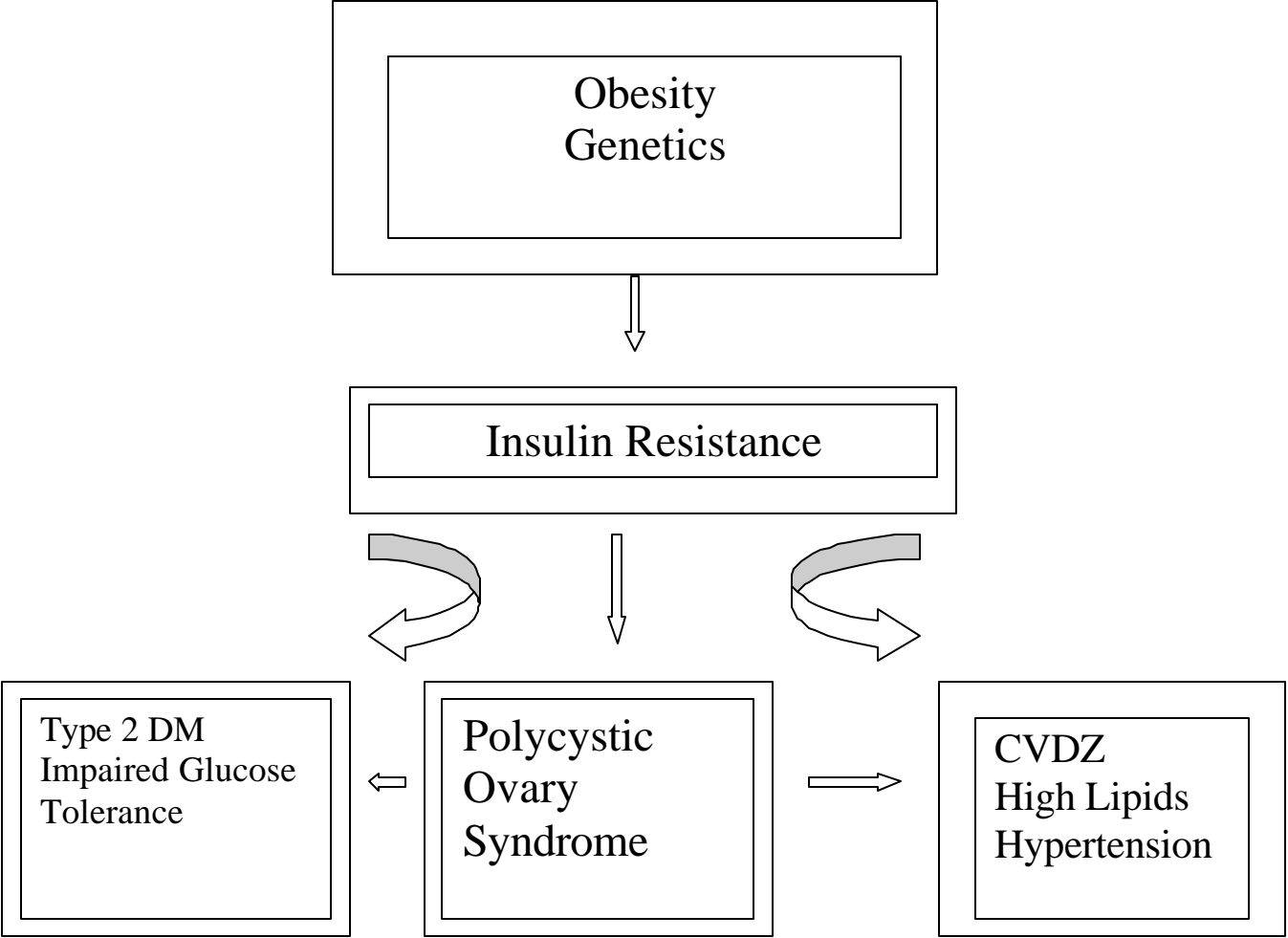
- Pregnancy
- Extreme or rapid weight changes, eating disorders
- Premature ovarian failure
- Pituitary adenoma
- Cushing's syndrome
- Androgenic Progestational agents
- Hyperthyroidism/hypothyroidism
- Adult onset congenital adrenal hyperplasia
- Ovarian or Adrenal tumors

## PCO Clues

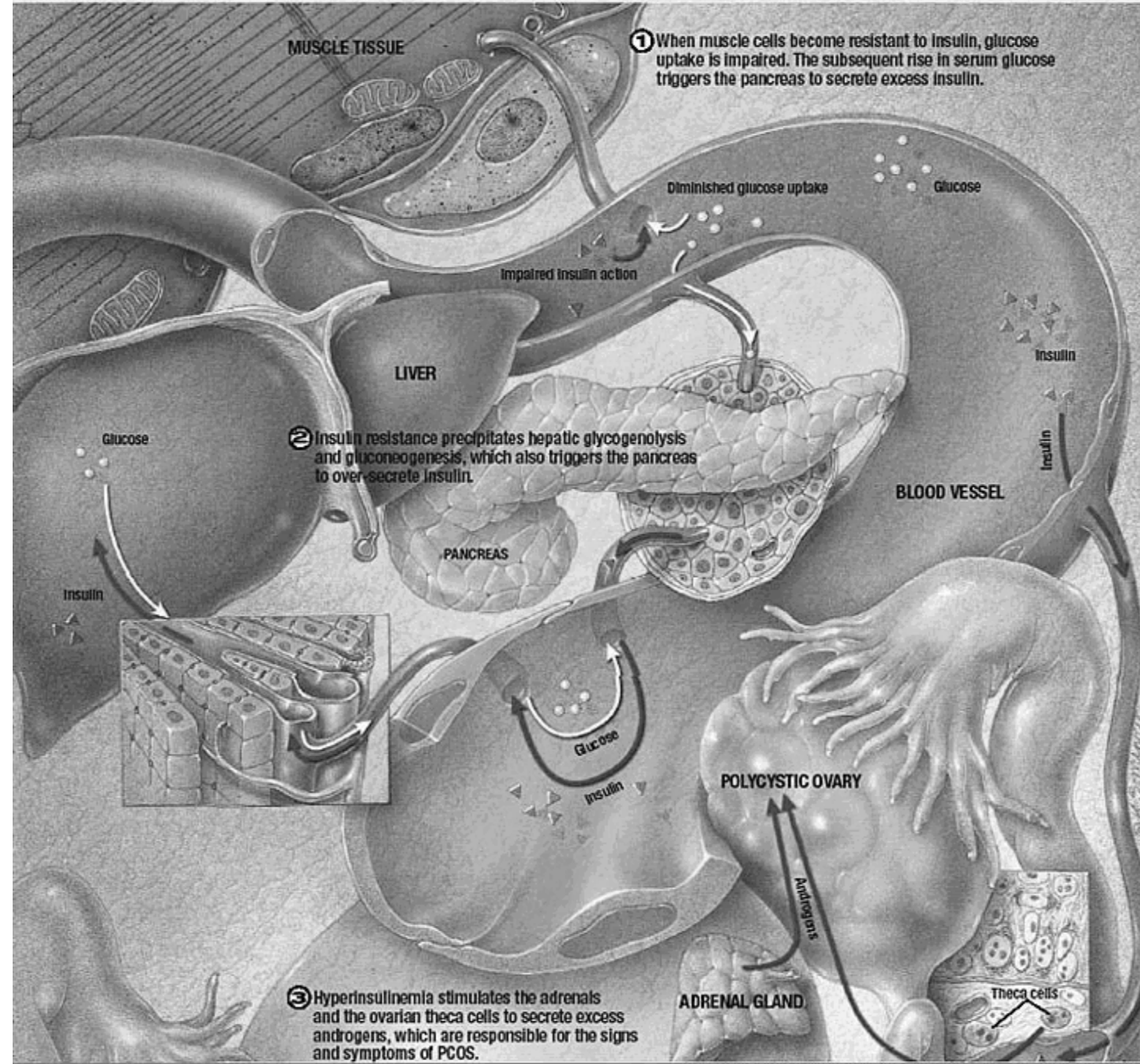
- Gradual onset of symptoms generally starting around puberty
- Family history of menstrual irregularity or hirsutism
- Family history of impaired glucose tolerance
- Central obesity

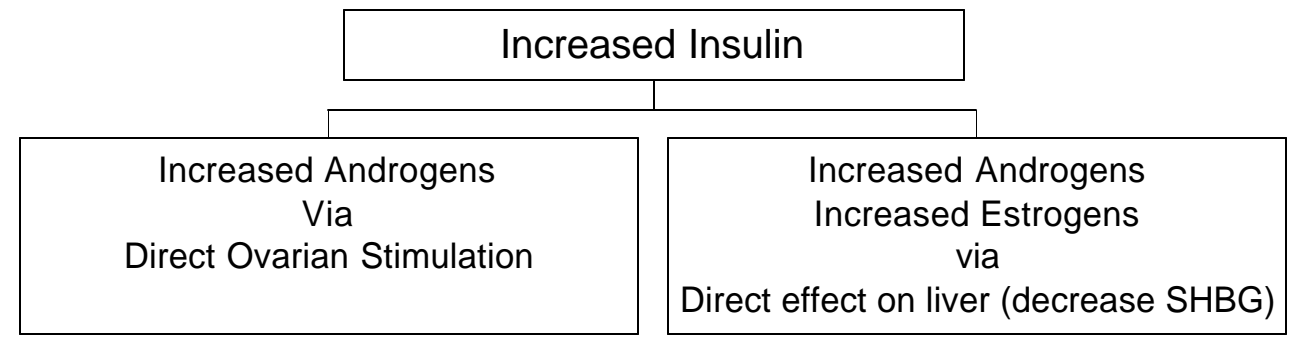
# Pathophysiology

- Likely a combination of factors
- Elevated insulin via insulin resistance
  - seems to directly and indirectly cause increased ovarian and adrenal androgens
  - occurs in obese and non-obese patients
- Abnormal GnRH pulsations via disordered steroid feed back loops
  - End result seems to be frequent follicle recruitment but no selection, ie anovulation

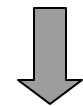


How insulin resistance contributes to PCOS

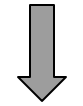




Altered GnRH pulse  
frequency and amount



FSH steady State, LH favored



Follicular recruitment, no selection, anovulation

# Evaluation

- Labs: rule out the obvious and the serious, then tailor the rest of the evaluation to the presentation
  - upreg
  - tsh, prl, LH, FSH
  - LH:FSH of 2:1 or greater used by some to dx, though not very sensitive

# Evaluation

- Rapid progression of androgenic symptoms may suggest androgenic tumor or adult onset CAH

## To rule out rare virilizing disorders

- Consider adding free and total testosterone, DHEAS, 17-hydroxyprogesterone
  - if your androgen level is slightly raised, supports pcos
  - if high, may support:
    - ovarian tumor (serum total testosterone >150 ng/L)
    - adrenal tumor (DHEAS >800 microgr/dl)
    - adult onset cah (post-corticotropin DHEAS level greater than 1000 ng/dl)

# Evaluation

- Obesity, moon facies, hypertension, striae, prox muscle weakness support cushings
  - Consider dexamethasone suppression test

# Evaluation

- Disagreement exists about whether to measure insulin sensitivity in pco patients
- There is no great way to do so outside of a lab with hyperinsulinemic-euglycemic clamps

## Why would you want to measure insulin sensitivity?

- Consideration could allow you to choose most appropriate therapy, monitor progress of treatment
- Consider insulin levels, fasting glucose, two hour glucose tolerance test, lipids

## How do you measure insulin sensitivity?

- Fasting Insulin Greater than 20 microunits/ml likely indicates resistance (may have some ethnic variation)
- Glucose/Insulin Ratio  $<4.5$  95% sensitive, 84% specific for insulin resistance in one study when women with pco compared with control group

# Evaluation

- Is there a role for ultrasound to diagnose polycystic ovarian syndrome?
  - No. Polycystic ovaries are not part of the definition of polycystic ovary syndrome.
  - 23% of non-pco women will have polycystic-appearing ovaries.
  - 80-100% of women with pco will have polycystic ovaries (generally small, peripherally oriented, 8-10 cysts)

# Complications

- Insulin Resistance
  - increased risk for DM Type II, Hypertension, lipid abnormalities, cardiovascular disease
- Endometrial hyperplasia
  - no ovulation, therefore unopposed estrogen
  - subset with endometrial atrophy secondary to androgen effect

# Complications

- Infertility
  - no ovulation
- Signs of Hyperandrogenism (especially hirsutism)
  - very upsetting to some patients

# Treatment

- Goals:
  - maintain cardiovascular health/reduce insulin resistance
  - maintain normal endometrium
  - correct anovulation (if fertility desired)
  - reduce androgen action on target tissue

## You might be able to do all in one fell swoop

- If insulin resistance is at the heart of the problem, diet and exercise might be able to resolve it all
- Study of 45 obese, Caucasian women with pco showed that 14.4% decrease in total body fat (across all women) improved lipid profile, insulin resistance and menstrual regularity.

# Insulin Resistance

- Diet and Exercise (10% weight loss)
- Metformin 500-850 tid, increase sensitivity and decrease hepatic gluconeogenesis.
- Helps hyperandrogenism, anovulation, and possibly the increased cardiovascular risk that may come along with increased insulin levels
- May take 4-6 months to see results

# Endometrial Health

- If pregnancy not desired can try OCPs :  
gives withdrawl bleeds and helps with  
androgenic effects peripherally
- Progesterone alone three times a year ok for  
endometrium
- Mirena IUD

# Hyperandrogenism

- Oral contraceptives
- Spironolactone 100-200 mg/day div bid
- Expect a response in 3-6 months
- Bleaching, wax stripping, shaving, electrolysis for hair growth
- Consider antibiotics for acne

# Infertility

- Metformin first line of treatment
- Clomid if no luck
- Ovarian drilling, ivf other options
- Send to REI clinic if no luck with first two

# My patient

- All initial lab studies normal
- Sent for fasting glucose, insulin levels, lipids
- Nutrition, lifestyle advice not working so well
- Plan to start metformin
- Will consider spironolactone